Estimating the healthcare costs of children born to pregnant smokers in England: cohort study using primary and secondary healthcare data.

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ABSTRACT

Background and aims

Little is known about the long term economic consequences of smoking during pregnancy. We estimated the association between smoking in pregnancy and the costs of delivering healthcare to infants and children, and investigated which aspects of care are the key drivers of these costs.

Methods

We used Hospital Episode Statistics (HES) linked with Clinical Practice Research Datalink (CPRD) data in England in children with longitudinal data for at least one, five and ten years after birth. Poisson regression provided rate ratios (RR) and 95% confidence intervals (CIs) comparing healthcare episode rates between those exposed and not exposed to smoking during pregnancy. Linear regression was used to compare estimated costs between groups (£ sterling, 2015 prices) and generalized linear multivariable (GLM) models adjusted for potentially moderating factors.

Results

A total of 93,152 singleton pregnancies with the required data were identified. Maternal smoking in pregnancy was associated with higher primary care, prescription and hospital inpatient episode rates, but lower outpatient visit and diagnostic test rates. Adjusting for year of birth, socio-economic deprivation, parity, sex of child and delivery method showed that maternal smoking in pregnancy was associated with increased child healthcare costs at 1 year (average cost difference for children of smokers, β: £91.18, 95%CI: £47.52-£134.83) and 5 years of age (β: £221.80, 95%CI: £17.78-£425.83), but not at 10 years of age (β: £365.94, 95%CI: -£192.72-£924.60).

Conclusion

Maternal smoking in pregnancy is associated with increased total healthcare utilisation and increased child healthcare costs over the first five years of life; these costs are primarily driven by increased numbers of hospital admissions.

INTRODUCTION

In Europe, the prevalence of smoking during pregnancy has been estimated to vary from 4.2% in Iceland to 18.9% in Croatia.(1) Maternal smoking during pregnancy is associated with many adverse infant and child outcomes, including an elevated risk of asthma, respiratory illness, sudden infant death syndrome (SIDS), behavioural difficulties (ADHD), preterm delivery and low birth weight, as well as poor maternal outcomes such as ectopic pregnancy and miscarriage.(2-4) These adverse sequelae are likely to increase the costs of health care for children born to pregnant smokers.

Few studies have quantified the additional burden on health care services for infants and children, which is attributable to smoking in pregnancy.(5-9) Godfrey et al. estimated the additional smoking-related costs to the UK National Health Service (NHS) incurred by infants during the first 12 months of life as between £12 and £23.5 million annually (2006 prices).(7) However, this work used literature-based estimates for costs arising from only selected morbidities believed to be associated with smoking rather than deriving cost estimates for all healthcare use. Petrou et al. used medical record linkage to investigate children's excess hospital inpatient costs attributable to smoking in pregnancy during their first five years of life,(9) and similarly other studies investigating this subject have been restricted to estimating specific elements of overall healthcare use such as neonatal intensive care admissions or health care during very early childhood.(5, 6, 8) We could find no studies which investigated infants' and children's healthcare costs attributable to smoking in pregnancy, which included a consideration of most healthcare episodes including those in hospital outpatient and primary care.

The primary aim of this paper was to estimate the impact of maternal smoking during pregnancy on the total cost of providing healthcare services for children. This was carried out using English data from the UK National Health Service (NHS), a public provider of care in England, Scotland, Wales and Northern Ireland. The government's annual NHS budget is over £90 billion and care is provided free at the point of use.(10) The structure varies in individual countries, but all provide primary (community care, General Practitioners, Pharmacists), secondary (hospital based access via referral) and tertiary (specialist hospital facilities) care.(10) We used long-term, comprehensive, prospective and routinely-collected data to investigate children's use and cost of general practitioner services, including consultations, prescriptions and diagnostic tests, along with hospital care services. Our secondary aim was to determine the distribution of costs borne by primary and secondary care providers.

METHODS

Data sources

UK-wide Clinical Practice Research Datalink (CPRD),(11) Hospital Episode Statistics (HES),(12) Office for National Statistics (ONS) mortality data(13) and Index of Multiple Deprivation (IMD) data were used (linked data provided by CPRD).(14) The study was approved by the CPRD Independent Scientific Advisory Committee (ISAC, protocol number: 15_186R). CPRD contains over 13 million anonymised primary care medical records from 684 UK general practices; prospectively collected records are available from 1987. Linked records are available for approximately 10 million patients in 398 practices. Linked HES inpatient data are available from 1997, linked HES outpatient data from 2003 and ONS mortality data from 1998 onwards. The IMD is an indicator of deprivation socioeconomic status (SES) based on census information from the patients' home postcodes grouped into lower super output areas (LSOA); each LSOA covers approximately 1500 residents/650 households.

Cohort of children born to pregnant smokers and non-smokers

We included children born in England following singleton pregnancies who had up-to-standard linked CPRD-HES data, with at least 1 year, 5 years or 10 years of follow-up from birth and whose mothers were aged 13-49 years at delivery. Mothers and children were identified first from the CPRD Mother-Baby link; we included women with a CPRD record of smoking status or use of smoking cessation medications in pregnancy. As records of smoking status in pregnancy are generally valid,(15) we were confident that using these attributions of exposure or non-exposure to smoking in pregnancy would be generally correct. The study ran from January 2003 until January 2015 when both inpatient and outpatient CPRD-linked HES data were available. Data on delivery method, parity, gestation and delivery dates, sex of the baby, and IMD were extracted from HES. Children's duration of follow-up was measured from birth until death, transfer out of a CPRD general practice or the end of the study period, whichever was earliest and individual children had data available for different lengths of time. To minimise any cluster effects, if a woman had more than one child during the follow-up period only one was randomly-selected for inclusion.

Exposure definitions

Smoking in pregnancy: Children were considered exposed to smoking in pregnancy when born to women who, between conception and delivery, had one or more smoking Medcodes or Multilex codes for smoking cessation medication prescriptions (i.e. NRT, Bupropion, Varenicline) recorded in CPRD. This method has been used previously in a study using The Health Improvement Network (THIN) database.(16)

Not smoking in pregnancy: Children were considered not exposed to smoking in pregnancy if their mother had a Medcode for being a non-smoker (including ex-smokers) recorded in CPRD during the gestational period. Consistent with the guidelines for attributing smoking status used by the UK Quality and Outcomes Framework (QOF),(17) women were also considered non-smokers if they were recorded as such at least three times before the age of 25, or before becoming pregnant, had been recorded as an ex-smoker in three or more consecutive years. Additionally, during pregnancy, women could not be issued with smoking pharmacotherapy prescriptions.

Primary care consultation costing

Different primary care events held with the a healthcare professional on the same date were classified as one consultation and costs were attributed to consultations using the 2015 Personal Social Services Research Unit (PSSRU) reference costs;(18) attribution was based on the type of healthcare professional providing the consultation (see below) and the consultation setting (i.e. Surgery, Home visit, Clinic, Out of hours, Telephone). Primary healthcare consultations were defined as those with GP partners/senior partners, registrars, locums or sole practitioners; community/practice nurses and dispensers/pharmacists. PSSRU unit costs include consultations' administrative costs, so consultations recorded as having been with administrative staff were excluded. Where the 2015 PSSRU unit cost compendium provided no unit cost for a provider and setting combination, this was instead taken from the most recent PSSRU unit cost compendia and adjusted to 2015 prices using the NHS Hospital and Community Health Services Pay and Price Index.(18)

Prescription costing

We recorded children's prescription items and used the British National Formulary (BNF) to cost prescriptions at the BNF chapter subparagraph level.(19) BNF chapters relate to body systems, BNF sections to prescribing for systems, and paragraph and subparagraph levels relate to the pharmacology and therapeutic use. The Prescription Cost Analysis (PCA) database for 2015(20) was used to attribute all prescription costs, irrespective of the year in which they were issued. Where the 2015 PCA database did not specify costs for items prescribed (32.3% of all prescriptions), the average 2015 PCA prescription cost (£30.96) was used.

Primary care diagnostic test costing

Children's diagnostic tests in the CPRD test file were identified and included. Costs for diagnostic tests were based on those listed in the National Schedule of Reference Costs (2015) for direct access pathology and diagnostic services.(18) Average costs were assigned for asthma tests (e.g. lung function/ spirometry), biochemistry (e.g. hormone, thyroid function, electrolytes), diabetic retinopathy, diagnostic imaging (e.g. chest x-ray), haematology (e.g. full blood count, clotting tests), microbiology (e.g. stool culture, sputum culture), histology, other pathology services (e.g. sputum cytology, urine cytology) and serology and immunology (e.g. immunoglobin tests, rubella/tuberculin tests). Individual costs, inflated to 2015 prices where necessary, were assigned to each diagnostic test (e.g. electrocardiogram, diagnostic bone marrow extraction etc.).

Secondary care costing

Secondary care encounters were derived from HES inpatient and outpatient data. HES inpatient data were extracted and each hospital admission was identified by a unique spell number. HES inpatient data were then reformatted to apply appropriate reference costs to admissions using the national tariff prices, based on the national average unit service provision costs taken from the 2015 National Schedule of Reference Costs.(18) This was achieved by using the hierarchical algorithm in the Health Resource Group (HRG) 4 2015/16 Local Payment Grouper programme,(21) provided by the Health and Social Care Information Centre (HSCIC). This programme applied HRG codes to care episodes, which were linked to NHS tariff costs.(18) HRG codes were generated for each episode of inpatient care experienced by children, and the sum of NHS tariff costs for these episodes was calculated for each child.

HES outpatient data were extracted by the CPRD Knowledge Centre.(11) 3.4% of outpatient episodes were costed using the HSCIC Grouper, while the majority (90.7%) of outpatient episodes were costed using treatment specialty average costs from the relevant NHS reference cost schedules. The remaining 5.9% of episodes had an average outpatient cost applied (£147.30) as they could not be costed by Grouper or treatment speciality. Reference costs for secondary NHS care in the UK are calculated on a full absorption costing basis and encompass staff salaries, on-costs, equipment, consumables and revenue and capital overheads.

Statistical Analysis

Our primary aim was to compare healthcare costs amongst children born to women who smoked and non-smokers in pregnancy within the first, the first five and the first 10 years of life; hence, findings are presented in cohorts with at least 1, 5 or 10 years of follow-up data available. Descriptive statistics of baseline maternal demographic characteristics for pregnancies were calculated, including the numbers of children with 1, 5 and 10 years of cohort data available, and the proportions of each born to smoking and non-smoking mothers.

Poisson regression was used to compute annualised rate ratios and 95% confidence intervals (CIs) for the association between smoking status and each component of primary and secondary healthcare. Numbers of primary and secondary care healthcare episodes used were collapsed into counts which were analysed cross-sectionally in these Poisson models. The analysis was stratified by factors considered to potentially affect children's health care use: maternal age (<20, 20-24, 25-29, 30-34 and ≥35 years), parity (0 or ≥1 children), socio-economic status (IMD quintiles), sex of infant (male, female) and mode of delivery (spontaneous, assisted, elective caesarean, emergency caesarean). Furthermore, year of birth was adjusted for to allow for the possibility that the volume and or pattern of health care provided to infants and children might have evolved through the course of each cohort, as well as the recorded prevalence of maternal smoking. As analyses employed multiple significance testing of strata on the same healthcare outcome, a Bonferroni correction was applied to tests at the 99.7% confidence level (i.e. $\alpha=0.05/19$, $p\leq0.003$, 19 = number of significance tests per outcome) to determine the significance of each association. The mean and standard deviations for the number of encounters were also calculated for each stratum.

Linear regression was used to compute coefficients and 95% CIs for the association between maternal smoking during pregnancy and the estimated costs of child healthcare utilisation, adjusting for year of birth. The absolute difference in average annual cost between children of smoking and non-smoking mothers was calculated. A similar Bonferroni correction was applied to the costs as to the previous analysis of healthcare utilisation. In supplementary material, findings are also presented in strata for maternal age, parity, socio-economic status, sex of child and delivery method. Since little is known about the costs attributable to smoking in primary and secondary care, especially beyond five years of follow up, this stratified analysis was carried out to present the findings in a descriptive way by these variables. Stratification of the follow-up into one, five and 10 year periods was chosen based on prior knowledge; costing in the first year is important, as utilisation during infancy may be associated with longer term costs. The first five years is a marker that is commonly used in the UK and by the WHO partially as children start formal schooling around age five and allows a comparison to other studies, and 10 year follow-up was the longest available with a significant number of participants to analyse.

In each cohort the variation in total health care costs for children of women who smoked in pregnancy, versus those who did not, was assessed using a multivariable generalised linear model (GLM) to generate cost coefficients and 95% CIs. The association between smoking in pregnancy and overall healthcare cost was adjusted for year of birth, maternal age, IMD, parity, sex of infant and mode of birth. A gamma distribution and fitted robust standard errors were applied. We further replicated the GLM models over one and five year time horizons, restricting the sample to those who had complete 10 year data, to investigate whether the effects of smoking during pregnancy waned or persisted in the reduced sample size with complete follow-up data.

Where data were missing for the stratification covariates for the multivariable models (maternal age, socio-economic status, parity, infant gender or mode of delivery) or for outcomes (described below), individuals were excluded from analyses. A comparative analysis investigating the distribution of the baseline covariates was performed to investigate whether removal of these cases biased the sample. Analyses were conducted using Stata 14.0 (Stata Corp., College Station, TX).

RESULTS

Cohort selection

There were 586,017 pregnancies with ‘up-to-standard’ CPRD-HES data from January 2003 onwards. 244,012 of these women had sufficient data to attribute smoking status within the pregnancy. 203,159 of these pregnancies had the minimum length of child follow-up (1 year). 137,737 of these children had the necessary HES-linked secondary care data and 44,585 children were randomly excluded as they were siblings and shared a mother. No participants were excluded due to there being missing data for other baseline maternal covariates. Therefore, the final cohort comprised 93,152 children, 21.8% of whom were born to women who had smoked in pregnancy.

Cohort characteristics

34,260 children had at least 5 years’ and 5,824 at least 10 years’ data. Approximately one fifth of children in 5 year and 10 year cohorts were children of maternal smokers. The largest proportion of mothers fell in the 30-34 year age range in each cohort. The proportions of children exposed to maternal smoking during pregnancy stratified by maternal age, IMD, parity, infant sex and mode of birth are listed in Table 1. In all three cohorts, women who smoked during pregnancy were, on average, younger and resided in more deprived areas. A slightly higher proportion of first time mothers smoked during pregnancy. A higher proportion of male children were contained in each of the follow-up cohorts and this did not differ by maternal smoking status. Finally, non-smoking mothers had a lower spontaneous vaginal delivery rate and a higher proportion had an instrumental delivery or a caesarean section; this may be attributable to the greater average age of mothers who did not smoke during pregnancy.

[Insert Table 1 here]

Comparison of healthcare utilisation by smokers' and non-smokers' children

Table 2 presents the adjusted annual rate ratios for primary and secondary care healthcare utilisation by children of smokers compared to non-smokers, stratified by length of follow-up (≥1 year, ≥5 years' and ≥10 years' follow-up) and adjusted for year of birth, maternal age, parity, SES, gender of child and delivery method. In the whole cohort, infants exposed to maternal smoking in pregnancy had higher primary care consultation (RR: 1.015, 95%CI: 1.007-1.022) and inpatient admission (RR: 1.040, 95%CI: 1.020-1.060) rates during the first year of life. In children for whom at least 5 years' data were available, those born to pregnant smokers had higher annual primary care (RR: 1.021, 95%CI: 1.005-1.038) and outpatient consultation (RR: 1.084, 95%CI: 1.036-1.134) rates, but a lower annual primary care diagnostic test rate (RR: 0.961, 95%CI: 0.924-0.999) during the first 5 years of life. Finally, in those with at least 10 years follow-up data, children born to pregnant smokers had higher annual primary care (RR: 1.062, 95%CI: 1.012-1.114) and outpatient consultation (RR: 1.126, 95%CI: 1.001-1.267) rates during the first 10 years of life. The risk ratios presented in Table 2 stratified by confounding factors, and Bonferroni-corrected, are presented in Supplementary Tables 1a-c.

[Insert Table 2 here]

Comparison of healthcare costs incurred by smokers' and non-smokers' children

Table 3 compares overall estimated health care costs incurred by children of women who smoked and did not smoke in pregnancy, disaggregating costs for different health care components. All associations were adjusted by year or birth, maternal age, parity, SES, gender of child and delivery method.

Smoking during pregnancy had the greatest influence on hospital inpatient costs, which were significantly greater for children whose mothers smoked during pregnancy (β: £93.95, 95%CI: £39.44-£148.45) during the first year of life. For all other aspects of health care utilisation (primary care, diagnostic tests, prescriptions, and outpatient care), including for the five and ten year cohorts, there were no significant differences in costs between the children whose mothers either smoked or didn't smoke during pregnancy. The coefficients presented in Table 3 stratified by confounding factors and Bonferroni-corrected, are presented in Supplementary Tables 2a-c.

[Insert Table 3 here]

Investigation of factors influencing costs: multivariable GLM model

Table 4 presents multivariable GLM models for children with at least 1, 5 and 10 years of follow-up data, with total healthcare costs as the dependant variable. Following adjustment for year of birth, IMD, parity, sex of child and delivery method, maternal smoking in pregnancy was associated with significantly higher total healthcare costs during the first (β: £91.18, 95%CI: £47.52-£134.83) and also the first 5 (β: £221.80, 95%CI: £17.78-£425.83) years of life, but not during the first 10 years (β: 365.94, 95%CI: -192.72-924.60). Over the first year of life, boys had greater total healthcare costs compared to girls (β: £229.05, 95%CI: £196.00-£262.10), whilst increasing intensity of intervention delivery method was also associated with greater costs (e.g. emergency caesarean β: £655.39, 95%CI: £599.96-£710.81). Greater socio-economic deprivation was associated with higher costs (5th IMD quintile: β: £79.03, 95%CI: £26.46-£131.61), but increasing maternal age was associated with lower total health care costs (e.g. for 30-34 year olds: β: -£117.16, 95%CI: -£167.58- -£66.74). Compared to complete cohort findings, total health care costs over the first 5 years and first 10 years of life showed similar associations with delivery mode, sex of child and IMD distribution. However, whilst maternal age showed little or no effect on total costs of child healthcare over extended follow-up periods, multiparity was associated with significantly reduced total healthcare costs over the first 10 years of life (-£645.09, 95%CI: -£1195.04- -£95.14).

[Insert Table 4 here]

Following restriction of the GLM models to children with complete 10 years follow-up data, the associations were similar to those for the unrestricted analysis at one year (β: 41.18, 95%CI: -£98.02- £180.38) and five years (β: £195.22, 95%CI: -£165.19- £555.63); however, the cost coefficients did not reach statistical significance.

Discussion

Infants and children of pregnant smokers had higher healthcare costs over the first five years of life, predominantly attributable to greater hospital inpatient care. Although rates of primary care consultations, hospital inpatient and hospital outpatient episodes were higher in smokers' children, our results indicate an inverse association between smoking during pregnancy and the number of diagnostic tests in primary care during the first five years of children's lives. This apparent underutilisation in the use of some primary health care services may reflect differences in health seeking behaviour between mothers characterised by different sociodemographic profiles, but this remains to be elucidated by future research studies in this clinical context.

Strengths and limitations

Amongst studies evaluating healthcare costs of children born to pregnant smokers, this has the longest follow-up and is the first to investigate costs after 5 years of life. Additionally, it is more comprehensive; we attempted to measure use of all healthcare rather than, as in previous studies, only assessing impacts generated by selected conditions thought to be associated with smoking in pregnancy (7) or taking only a secondary care perspective.(9) We believe this work is the first to use multivariable methods to identify key influences on children's smoking-attributable healthcare costs.

A limitation is that we defined the smoking status in pregnancy from records of tobacco use and of smoking cessation medication prescriptions in medical records and this involved some assumptions. Some women stop smoking later in pregnancy but our simplified classification of women as either 'smoking' or 'not smoking' for the whole of pregnancy could not reflect this and some women may have been categorised as smoking throughout pregnancy when they may only have smoked briefly. However, patients usually provide accurate information to General Practitioners and we have previously demonstrated that assumptions used in this study lead to valid attribution of smoking status (15), so any misclassification of smoking will be small and study findings are likely to be valid. Additionally, as misclassification would tend to reduce apparent differences between groups' healthcare cost estimates, findings are conservative and actual cost differences may be larger. A further limitation was the absence of comprehensive data on the number of cigarettes smoked during pregnancy. As data on this variable were only available in the records of 22% of women, we did not account for this factor as this would have reduced the sample size and precision of estimates, especially for the analyses over an extended time horizon for which we had fewer complete cases.

As women who smoke in pregnancy are likely to smoke after childbirth, some of infants' and children's healthcare use in the smoking-exposed group may be attributable to second hand smoking (SHS). We decided not to attempt to factor this into our analyses as smoking data were inconsistently recorded at varied time points and even where these data were available it was not possible to ascertain whether infants' exposure to parental smoking had occurred. Although the extent of children's SHS exposure in this cohort is not known, we do not anticipate that this will have a marked effect, as in the UK since 2007, the percentage of children exposed to SHS for 'at least one hour a week' has remained static at about 11%.(22) SHS exposure may have been more prevalent at the start of the cohort but it seems unlikely that this will have had a substantial impact on findings; nevertheless, our cost estimates are probably best viewed as those which could be avoided if smoking in pregnancy was permanently eliminated and women remained abstinent after childbirth.

We cannot discount the possibility that there are unobserved clinical and behavioural characteristics that are positively correlated with both smoking in pregnancy and economic outcomes and not accounting for them in the models may have biased upwards the apparent effect of smoking. A number of clinical conditions that increase the risk of poor birth outcomes with long-term sequelae, such as gestational hypertension,(23, 24) are likely to have been present with the sample. Similarly, we did not adjust for other risky behaviours associated with smoking in pregnancy such as illicit drug or alcohol use. Illicit drug use is not recorded reliably in routinely collected electronic medical records and may be treated in specialist facilities not covered by primary and secondary care records, whilst the GP enhanced services contract provides an opt-out clause to not be involved in the treatment of drug dependence.(25) As a result, drug dependence could have been differentially recorded during the study period and thus we could not adjust for it reliably. Similarly, alcohol use during pregnancy is poorly recorded and has low prevalence (6.8%)(26) and there is some evidence of systematic misclassification in routinely recorded data by doctors.(27) Therefore, the effects of illicit drug and alcohol use were not explicitly accounted for. However, drug and alcohol related problems are very strongly associated with socio-economic deprivation, and we did adjust for this in the form of IMD scores in all of our analyses, which as a proxy for these factors may have reduced this bias.

Another limitation derives from linked HES data only having being available for 12 years resulting in relatively few children having 10 years' follow-up data, a comparatively small 10-year cohort and analyses at this time point having limited power. Restricting the analyses for total costs at one and five years to a group with 10 year follow-up data found that, although the associations were similar to those for the unrestricted analysis, the cost coefficients did not reach statistical significance. This may have been due to an insufficient sample size rather than a proven waning of the effect of smoking during pregnancy. Future, bigger studies might be necessary for a more definitive investigation of findings at 10-year follow up. Nevertheless, this cohort has a substantially longer follow-up period than the previous longest study and as such is a substantial contribution to the literature.(9)

Results in context

Petrou et al. estimated mean hospital inpatient cost differences between children born to smokers and non-smokers as £138, £307 and £462 over the first 5 years of life in women who reported smoking 1-9, 10-19 or ≥20 cigarettes, respectively.(9) Although these cost estimates were derived from hospital inpatient data extracted from a limited geographical area of England (Oxford Record Linkage Study), they are broadly similar in magnitude to the mean total healthcare cost differences we generated (multivariable model at 5 years: £221.80 (£17.78-£425.83)). This may reflect our finding that overall healthcare costs were most strongly influenced by hospital admissions. Godfrey et al. investigated average costs for maternal outcomes and infant outcomes attributable to smoking and non-smoking in pregnancy.(7) Using literature based unit costs, infant outcomes over the first year of life related to smoking in pregnancy were estimated to cost the NHS £12-£23.5 million per year. Our multivariable model generated a mean incremental child healthcare cost attributable to maternal smoking during pregnancy of £91.18 (£47.52-£134.83) over the first year of life. Assuming approximately 700,000 pregnancies per year and a UK prevalence of smoking during pregnancy of 15%(28, 29) this translates to an additional annual health care cost of £9.6 (£4.9-£14.1) million when the health sequelae of smoking during pregnancy are restricted to those experienced during the first year of life. This represents a more conservative estimate of costs attributable to smoking during pregnancy compared to those derived from the published literature. When the health sequelae of smoking during pregnancy are extended to the first 5 years of life, additional annual health care costs increase to £23.3 (£1.9-£44.7) million. Overall findings from this direct analysis of health care use suggest that excess infant health care costs attributable to maternal smoking in pregnancy are smaller than previously estimated. Actual costs could be higher or lower than point estimates though because, as previously noted, biases within analyses might inflate or reduce the derived point estimates.

Although health benefit remains the principal reason for encouraging smoking cessation in pregnancy, findings suggest that smoking cessation in pregnancy is also likely to lessen the costs of providing healthcare to children. When assessing the potential economic benefits of providing stop smoking services for pregnant women, any reduction in maternal healthcare costs associated with smoking during pregnancy should be considered in addition to the infant and childhood ones we have quantified. For example, recent estimates suggest that English NHS Stop Smoking Services cost £235 per quitter (29) so most of the investment made providing such services could be recouped in the medium term by the reduced spending on infant's and children's health care generated by the smoking cessation which these services promote. Indeed, adding in any reductions in the costs of providing healthcare to pregnant women who stop smoking permanently, the provision of cessation support in pregnancy could even be cost-saving to a health system.

Conclusions

Maternal smoking in pregnancy is a leading preventable cause of harm to mothers and babies, and we found that it is associated with increased children's healthcare costs over the first 5 years of life, with elevated costs primarily driven by more costly hospital admissions. Findings imply that funding cessation support for pregnant smokers could have economic benefits in addition those health benefits which accrue from permanent smoking cessation in pregnancy.

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Table 1. Maternal and child characteristics according to mother's smoking status during pregnancy

	At least 1 year's follow-up†		At least 5 years' follow-up		At least 10 years' follow-up	
	Non-smokers (%)	Smokers (%)	Non-smokers (%)	Smokers (%)	Non-smokers (%)	Smokers (%)
Overall	72863 (78.2)*	20289 (21.8)*	26958 (78.7)*	7302 (21.3)*	4666 (80.1)*	1158 (19.9)*
Maternal age (years)						
<20	2475 (3.4)	2188 (10.8)	797 (3.0)	790 (10.8)	121 (2.6)	105 (9.1)
20-24	9298 (12.8)	5548 (27.3)	3178 (11.8)	1879 (25.7)	538 (11.5)	273 (23.6)
25-29	19352 (26.6)	5516 (27.2)	6693 (24.8)	1871 (25.6)	1128 (24.2)	304 (26.3)
30-34	24690 (33.9)	4368 (21.5)	9224 (34.2)	1655 (22.7)	1668 (35.8)	305 (26.3)
≥35	17048 (23.4)	2669 (13.2)	7066 (26.2)	1107 (15.2)	1211 (26.0)	171 (14.8)
Socio-economic status: Index of Multiple Deprivation						
1 (least deprived)	18142 (24.9)	2585 (12.7)	7550 (28.0)	1019 (14.0)	1442 (30.9)	174 (15.0)
2	15735 (21.6)	3195 (15.8)	6053 (22.5)	1203 (16.5)	1110 (23.8)	197 (17.0)
3	13872 (19.0)	3855 (19.0)	5028 (18.7)	1376 (18.8)	864 (18.5)	232 (20.0)
4	13789 (18.9)	4968 (24.5)	4668 (17.3)	1788 (24.5)	735 (15.8)	278 (24.0)
5 (most deprived)	11325 (15.5)	5686 (28.0)	3659 (13.6)	1916 (26.2)	515 (11.0)	277 (23.9)
Parity						
0	42358 (58.1)	12370 (61.0)	11774 (43.7)	3370 (46.2)	1842 (39.5)	461 (39.8)
≥1	30505 (41.9)	7919 (39.0)	15184 (56.3)	3932 (53.9)	2824 (60.5)	697 (60.2)
Sex of child						
Female	34585 (47.5)	9620 (47.4)	12533 (46.5)	3411 (46.7)	2107 (45.2)	543 (46.9)
Male	38278 (52.5)	10669 (52.6)	14425 (53.5)	3891 (53.3)	2559 (54.8)	615 (53.1)
Delivery method						
Spontaneous vaginal delivery	42756 (58.7)	13068 (64.4)	15999 (59.4)	4736 (64.9)	2729 (58.5)	756 (65.3)
Assisted delivery	10693 (14.7)	2513 (12.4)	3491 (13.0)	848 (11.6)	618 (13.2)	126 (10.9)
Elective caesarean	7769 (10.7)	1724 (8.5)	3178 (11.8)	658 (9.0)	575 (12.3)	108 (9.3)
Emergency caesarean	11645 (16.0)	2984 (14.7)	4290 (15.9)	1060 (14.5)	744 (16.0)	168 (14.5)

*Row percentage, otherwise column percentage

†Follow-up at one year constitutes entire study cohort

Table 2. Adjusted annual rate ratios for primary and secondary healthcare utilisation for children whose mothers were smokers compared to non-smokers during pregnancy

	Number of Primary Care consultations, Mean (Median)			95% CI	
	Non-smoking	Smoking	RR*	lower	upper
(0-1 years follow-up for those with at least 1 year follow-up data) (N=93,152)	12.17 (10)	12.36 (11)	**1.015**	**1.007**	**1.022**
(0-5 years follow-up for those with at least 5 years follow-up data) (N=34,260)	31.59 (27)	32.17 (27)	**1.021**	**1.005**	**1.038**
(0-10 years follow-up for those with at least 10 years follow-up data) (N=5,824)	42.73 (35)	45.57 (37)	**1.062**	**1.012**	**1.114**
	Number of prescriptions, Mean (Median)			95% CI	
	Non-smoking	Smoking	RR*	lower	upper
(0-1 years follow-up for those with at least 1 year follow-up data) (N=93,152)	5.04 (3)	5.15 (3)	1.005	0.994	1.016
(0-5 years follow-up for those with at least 5 years follow-up data) (N=34,260)	15.62 (10)	15.45 (11)	0.980	0.959	1.003
(0-10 years follow-up for those with at least 10 years follow-up data) (N=5,824)	23.71 (15)	24.64 (17)	1.016	0.953	1.084
	Number of diagnostic tests, Mean (Median)			95% CI	
	Non-smoking	Smoking	RR*	lower	upper
(0-1 years follow-up for those with at least 1 year follow-up data) (N=93,152)	2.26 (1)	2.19 (1)	0.990	0.974	1.006
(0-5 years follow-up for those with at least 5 years follow-up data) (N=34,260)	5.56 (1)	5.32 (1)	**0.961**	**0.924**	**0.999**
(0-10 years follow-up for those with at least 10 years follow-up data) (N=5,824)	9.33 (2)	9.98 (3)	1.078	0.974	1.193
	Inpatient, Mean (Median)**			95% CI	
	Non-smoking	Smoking	RR*	lower	upper
(0-1 years follow-up for those with at least 1 year follow-up data) (N=93,152)	1.54 (1)	1.63 (1)	**1.040**	**1.020**	**1.060**
(0-5 years follow-up for those with at least 5 years follow-up data) (N=34,260)	2.09 (1)	2.27 (1)	1.048	0.986	1.114
(0-10 years follow-up for those with at least 10 years follow-up data) (N=5,824)	2.38 (1)	2.60 (2)	1.062	0.869	1.298
	Outpatient, Mean (Median)**			95% CI	
	Non-smoking	Smoking	RR*	lower	upper
(0-1 years follow-up for those with at least 1 year follow-up data) (N=93,152)	1.11 (0)	1.07 (0)	1.004	0.981	1.028
(0-5 years follow-up for those with at least 5 years follow-up data) (N=34,260)	3.84 (1)	4.13 (1)	**1.084**	**1.036**	**1.134**
(0-10 years follow-up for those with at least 10 years follow-up data) (N=5,824)	6.65 (2)	7.63 (3)	**1.126**	**1.001**	**1.267**

*Poisson regression RR (95%CI) for number of consultations per year of follow-up, adjusted for year of birth, maternal age, parity, SES, gender of child and delivery method

** Secondary care consultations

Risk ratios in **bold font** are significant at **p≤0.003**

Table 3. Primary care, secondary care and overall costs of healthcare utilisation accrued for children whose mothers were smokers compared to non-smokers during pregnancy

	Cost of Primary Care consultations, Mean (Median)*			95% CI	
	Non-smoking	Smoking	β	lower	upper
Costs for children at 1 year with at least 1 year of follow-up (N=93,152)	192 (166)	193 (167)	1.11	-1.86	4.07
Costs for children at 5 years with at least 5 years of follow-up (N=34,260)	508 (435)	513 (440)	6.97	-6.60	20.56
Costs for children at 10 years with at least 10 years of follow-up (N=5,824)	705 (592)	742.12 (634)	31.62	-16.59	79.84
	Cost of prescriptions, Mean (Median)*			95% CI	
	Non-smoking	Smoking	β	lower	upper
Costs for children at 1 year with at least 1 year of follow-up (N=93,152)	324 (177)	330 (187)	0.30	-11.81	12.40
Costs for children at 5 years with at least 5 years of follow-up (N=34,260)	1063 (588)	1060 (617)	-6.51	-85.10	72.08
Costs for children at 10 years with at least 10 years of follow-up (N=5,824)	1781 (868)	1847 (1028)	29.84	-362.67	422.36
	Cost of diagnostic tests, Mean (Median)*			95% CI	
	Non-smoking	Smoking	β	lower	upper
Costs for children at 1 year with at least 1 year of follow-up (N=93,152)	21 (0)	22 (0)	1.72	-0.27	3.71
Costs for children at 5 years with at least 5 years of follow-up (N=34,260)	56 (4)	56 (1)	0.24	-6.88	7.36
Costs for children at 10 years with at least 10 years of follow-up (N=5,824)	124 (14)	126 (14)	0.18	-40.77	41.14
	Inpatient, Mean (Median)*			95% CI	
	Non-smoking	Smoking	β	lower	upper
Costs for children at 1 year with at least 1 year of follow-up (N=93,152)	755 (0)	862 (0)	**93.95**	**39.44**	**148.45**
Costs for children at 5 years with at least 5 years of follow-up (N=34,260)	1299 (0)	1526 (604)	173.41	-44.83	391.65
Costs for children at 10 years with at least 10 years of follow-up (N=5,824)	1620 (595)	1841 (731)	152.69	-489.51	794.90
	Outpatient, Mean (Median)*			95% CI	
	Non-smoking	Smoking	β	lower	upper
Costs for children at 1 year with at least 1 year of follow-up (N=93,152)	189 (0)	183 (0)	3.06	-8.62	14.73
Costs for children at 5 years with at least 5 years of follow-up (N=34,260)	605 (193)	659 (193)	52.58	-5.47	110.62
Costs for children at 10 years with at least 10 years of follow-up (N=5,824)	1014 (382)	1181 (500)	135.10	-81.34	351.54

*regression coefficients for cost (£) adjusted for year of birth, maternal age, SES, parity, gender of child and delivery method
Coefficients in **bold font** are significant at **p≤0.003**

Table 4. Multivariable GLM models for total costs incurred by 1 year, 5 years and 10 years follow-up

Variables	Total Costs, 0-1 years (N=93,152)				Total Costs, 0-5 years (N=34,260)				Total Costs, 0-10 years (N=5,824)			
		95% CI				95% CI				95% CI		
	β	lower	upper	p<0.05	β	lower	upper	p<0.05	β	lower	upper	p<0.05
Maternal smoking during pregnancy	**91.18**	**47.52**	**134.83**	**<0.001**	**221.80**	**17.78**	**425.83**	**0.033**	365.94	-192.72	924.60	0.199
Year of birth	25.43	20.03	30.84	<0.001	10.96	-25.49	47.41	0.556	-221.99	-613.69	169.71	0.267
Maternal age (years)												
<20	72.12	-52.03	196.26	0.255	268.01	-204.67	740.68	0.266	929.13	-515.37	2373.63	0.207
20-24	0.00	-	-	-	0.00	-	-	-	0.00	-	-	-
25-29	**-86.11**	**-137.64**	**-34.59**	**0.001**	-176.53	-462.52	109.46	0.226	275.07	-413.62	963.77	0.434
30-34	**-117.16**	**-167.58**	**-66.74**	**<0.001**	**-273.43**	**-542.96**	**-3.91**	**0.047**	-46.98	-638.91	544.95	0.876
≥35	-54.26	-112.71	4.19	0.069	-75.41	-365.00	214.19	0.610	-50.04	-773.58	673.50	0.892
Socio-economic status: Index of Multiple Deprivation												
1 (least deprived)	0.00	-	-	-	0.00	-	-	-	0.00	-	-	-
2	**67.83**	**17.18**	**118.48**	**0.009**	-114.12	-305.36	77.12	0.242	111.25	-562.81	785.30	0.746
3	18.74	-28.97	66.45	0.441	87.01	-151.44	325.46	0.474	0.02	-732.92	732.97	1.000
4	18.07	-32.78	68.92	0.486	96.77	-131.51	325.05	0.406	289.73	-394.88	974.35	0.407
5 (most deprived)	**79.03**	**26.46**	**131.61**	**0.003**	**295.80**	**56.61**	**534.98**	**0.015**	**996.54**	**205.62**	**1787.46**	**0.014**
Parity												
0	0.00	-	-	-	0.00	-	-	-	0.00	-	-	-
≥1	25.63	-9.54	60.80	0.153	95.50	-49.02	240.02	0.195	**-645.09**	**-1195.04**	**-95.14**	**0.022**
Sex of child												
Female	0.00	-	-	-	0.00	-	-	-	0.00	-	-	-
Male	**229.05**	**196.00**	**262.10**	**<0.001**	**465.22**	**320.74**	**609.70**	**<0.001**	**1140.25**	**650.11**	**1630.40**	**<0.001**
Delivery method												
Spontaneous vaginal delivery	0.00	-	-	-	0.00	-	-	-	0.00	-	-	-
Assisted delivery	**299.98**	**247.48**	**352.47**	**<0.001**	**619.49**	**364.87**	**874.11**	**<0.001**	588.17	-116.89	1293.23	0.102
Elective caesarean	**371.81**	**304.12**	**439.49**	**<0.001**	**886.30**	**583.07**	**1189.53**	**<0.001**	704.27	-21.35	1429.88	0.057
Emergency caesarean	**655.39**	**599.96**	**710.81**	**<0.001**	**1275.37**	**1022.32**	**1528.42**	**<0.001**	**1483.91**	**679.90**	**2287.91**	**<0.001**